

REMARKS

The specification has been amended to correct obvious typographical errors. Claims 2, 3, 4, 11, 12, 14, 15, 16, 17, 34-35, 37-38, and 40-41 have been cancelled without prejudice. Claims 1, 13, 18, 24, 36, and 39 have been amended. Support for these amendments may be found in Figures 24-25 and throughout the specification, *e.g.*, page 5, lines 1-9 and page 41, lines 8-11. New Claims 42-44 have been added. Support for the new claims may be found throughout the specification, *e.g.* page 17, lines 1-7. No new matter is introduced by these amendments or new claims. As such, with this response, claims 1, 13, 18-33, 36, 39, and 42-44 are currently pending.

I. Restriction Requirement

Applicants acknowledge the finality of the restriction requirement but maintain their traversal. The Office Action states that the restriction remains proper because "...databases and resource allocation at the PTO have changed such that the examination of more than one sequence on the merits in the instant application would present a burden on PTO resources." Office Action at page 2. However, the Office has submitted no proof that such a serious burden would be imposed by a search and examination of all of the recited SEQ ID NOs. Applicants have, however, cancelled claims to non-elected sequences.

II. Rejection under 35 U.S.C. §112, 1st Paragraph: Written Description

Claims 1-4, 11-12, 13-18, 34, 36, and 39¹ were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Office Action at page 3. Applicants respectfully traverse this rejection.

The Examiner acknowledges that the specification "discloses the structure of the *Arabidopsis* aromatic prenyltransferase nucleic acid sequence of the elected invention, SEQ ID NO: 1, and that this nucleic acid encodes a functional protein as evidenced by its ability to

¹ Applicants have cancelled claims 2-4, 11-12, 14-17, and 34 without prejudice to facilitate prosecution. Claims 1, 13, 18, 36, and 39 therefore stand rejected under 35 U.S.C. §112

complement a *Synechocystis* knockout mutant.” Office Action at page 3. However, the Examiner asserts that “the specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids.” Office Action at page 3.

Applicants thank the Examiner for the acknowledgement that the specification discloses the structure of the *Arabidopsis* aromatic prenyltransferase nucleic acid sequence of the elected invention, SEQ ID NO: 1, and that this nucleic acid encodes a functional protein, but respectfully disagree with the Examiner’s conclusion.

An adequate written description of a genus of nucleic acids may be achieved by either “a recitation of a representative number of [nucleic acid molecules], defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus.” *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69 (Fed. Cir. 1997). This Applicants have done.

For example, Applicants have disclosed seven putative *Arabidopsis* prenyltransferases of the straight-chain class: ATPT1 (SEQ ID NO: 9), ATPT7 (SEQ ID NO: 10), ATPT8 (SEQ ID NO: 11), ATPT9 (SEQ ID NO: 13), ATPT10 (SEQ ID NO: 14), ATPT11 (SEQ ID NO: 15), and ATPT12 (SEQ ID NO: 16), and five putative prenyltransferases of the aromatic class: ATPT2 (SEQ ID NO: 1), ATPT3 (SEQ ID NO: 3), ATPT4 (SEQ ID NO: 5), ATPT5 (SEQ ID NO: 7), and ATPT6 (SEQ ID NO: 8). *See* Specification, page 22, lines 25-30. Applicants have also disclosed aromatic prenyltransferase sequences from soy (SEQ ID NOs: 19-23), from maize (SEQ ID NOs: 25-29 and 31), and from *Synechocystis* (SEQ ID NOs: 32, 33, 34, 35, 36, and 38). *See* Specification, page 22, line 30 to page 23, line 4, page 30 lines 7-14, and page 37, lines 2-3.

As such, Applicants have provided a representative number of nucleic acid sequences and have provided experimental evidence that such sequences encode a functional protein. Further, Applicants have provided a structural characteristic of the elected sequence through SEQ ID NO: 1. As such, Applicants have satisfied the *Eli Lilly* test for adequate written description.

Based on the foregoing, it is clear that one of ordinary skill in the art would recognize that Applicants were in possession of the claimed invention. Therefore, it is respectfully submitted that the rejection under 35 U.S.C. §112, 1st paragraph, written description, is improper and should be withdrawn.

III. Rejection under 35 U.S.C. §112, 1st Paragraph: Enablement

Claims 1-4 and 11-41² also stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled. The Examiner acknowledges that a method of increasing tocopherol content in *Arabidopsis* seeds and a method of increasing the level of alpha tocopherol content in the *Synechocystis* knockout mutant slr1763 are enabled. However, the Examiner asserts that the specification “does not reasonably provide enablement for other methods using other isolated nucleic acids encoding other prenyltransferases.” Office Action at page 4. Applicants respectfully traverse this rejection.

The present specification discloses how to make and use the claimed invention (*e.g.*, identifying prenyltransferase sequences, preparing expression constructs, transforming plants, identifying additional prenyltransferases, and analyzing transgenic plants). *See, e.g.*, Examples 1-5. The specification discloses many examples of sequences that can be used to transform various host cells. *See* specification, Example 2. The specification also discloses examples of cells and plants that have been transformed with the sequences of the present invention. *See, e.g.*, specification, Example 2 and Example 5. Further, transgenic plants having seeds with increased tocopherol levels are shown. *See* specification, Example 5.

Moreover, the Examiner has not met the evidentiary burden to impose an enablement rejection. A specification that discloses how to use a claimed invention “must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein.” *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), *quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original). However, the Examiner has provided neither specific evidence supporting the rejection nor any explanation of why the specification allegedly fails to enable a nucleic acid molecule encoding a prenyltransferase, particularly in light of the extensive teaching with Applicant’s specification. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) (“pure conjecture” does not substantiate rejection for lack of enablement).

² Applicants have cancelled claims 2-4, 11-12, 14-17, 34-35, 37-38, and 40-41 without prejudice to facilitate prosecution. Claims 1, 13, 18-33, 36, and 39 therefore stand rejected under 35 U.S.C. § 112, first paragraph.

The Office Action asserts that undue experimentation would be required to make and use the invention as it is claimed. Office Action at page 5, paragraph 18. Applicants respectfully disagree. The Examiner relies on Shewmaker *et al.* and Burkhardt *et al.*, apparently suggesting that those references teach unpredictability in the art of the present invention. Office Action at page 5 paragraph 18. On the basis of Shewmaker *et al.* and Burkhardt *et al.*, the Examiner concludes that “[g]iven the unpredictability of any isolated nucleic acid encoding a prenyltransferase to functionally substitute for SEQ ID NO: 1, the absence of guidance in the specification for making and using other isolated nucleic acid encoding functional prenyltransferases, the lack of working examples, and given the breadth of the claims which encompass any nucleic acid encoding any prenyltransferase as well as methods involving said nucleic acid sequences, it would require undue experimentation by one skilled in the art to make and /or use the claimed invention.” Office Action at page 5, paragraph 18.

The Examiner, however, fails to acknowledge the teachings set forth in the specification. As described above in detail, the present specification discloses how to make and use the present invention. More particularly, Applicants have disclosed the structure of several prenyltransferase nucleic acid sequences that can be used in the various embodiments of the present invention. For example, Applicants have disclosed seven putative *Arabidopsis* prenyltransferases of the straight-chain class: ATPT1 (SEQ ID NO: 9), ATPT7 (SEQ ID NO: 10), ATPT8 (SEQ ID NO: 11), ATPT9 (SEQ ID NO: 13), ATPT10 (SEQ ID NO: 14), ATPT11 (SEQ ID NO: 15), and ATPT12 (SEQ ID NO: 16), and five putative prenyltransferases of the aromatic class: ATPT2 (SEQ ID NO: 1), ATPT3 (SEQ ID NO: 3), ATPT4 (SEQ ID NO: 5), ATPT5 (SEQ ID NO: 7), and ATPT6 (SEQ ID NO: 8). *See* Specification, page 22, lines 25-30. Applicants have also disclosed aromatic prenyltransferase sequences from soy (SEQ ID NOs: 19-23), from maize (SEQ ID NOs: 25-29 and 31), and from *Synechocystis* (SEQ ID NOs: 32, 33, 34, 35, 36, and 38). *See* Specification, page 22, line 30 to page 23, line 4, page 30 lines 7-14, and page 37, lines 2-3.

The specification also discloses how to select genes (*e.g.*, Example 1, page 22 line 17 through page 24 line 9, and page 8 lines 9-14), how to construct vectors and transform plants (*e.g.*, page 12 line 26 – page 20, line 22). In addition, the specification details methods for confirming increased tocopherol levels. *See, e.g.*, Example 5 page 41 line 6 through page 42 line

26, Figure 24. The Examiner has not indicated how either Shewmaker *et al.* or Burkhardt *et al.* suggest that such work would be “undue experimentation.”

As such, based on the extensive teachings of the specification and the high level of skill in the art, the enablement requirement has been met. On the basis of the foregoing, Applicants respectfully request that the Examiner withdraw the enablement rejection under 35 U.S.C. §112, first paragraph.

IV. Rejection under 35 U.S.C. §112, 2nd Paragraph, Indefiniteness

Claims 19, 24, and 29 stand rejected under 35 U.S.C. §112, 2nd paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Office Action at page 6.

Claim 19 was rejected because the term “alteration” allegedly renders the claim indefinite because it is unclear “in what way the tocopherol content of the host cell is altered.” Office Action at page 6. This rejection is respectfully traversed. One of ordinary skill in the art would be able to ascertain the metes and bounds of the term “alteration” based on the teachings of the specification. For instance, the specification describes “methods for altering (for example, increasing and decreasing) the tocopherol levels and/or modulating their ratios in host cells.” Specification at page 5, line 14-16. One of ordinary skill in the art would therefore recognize the term “alteration” as reflecting any change in the total or relative amounts of tocopherol compounds.

As such, it is submitted that claim 19 complies with 35 U.S.C. § 112, 2nd paragraph, and withdrawal of this rejection is respectfully requested.

Claim 24 was rejected because the phrase “a tocopherol of interest” allegedly renders the claim indefinite because it is “unclear what tocopherols are encompassed by the claim.” Office Action at page 6. Applicants disagree that “a tocopherol of interest” is indefinite. However to facilitate prosecution, Applicants have amended claim 24 to remove the phrase “of interest.”

As such, it is submitted that claim 24 complies with 35 U.S.C. § 112, 2nd paragraph, and withdrawal of this rejection is respectfully requested.

Claim 29 was rejected because the phrase “increasing the biosynthetic flux in a host cell toward tocopherol” allegedly renders the claim indefinite because it is “unclear what constitutes

increasing the biosynthetic flux in a host cell toward tocopherol.” Office Action at page 6. Applicants disagree that claim 29 is indefinite or vague, and respectfully point out that claims are to be read in light of the specification. *See In re Vogel*, 422 F.2d 438, 441, 164 U.S.P.Q. 619, 622 (C.C.P.A. 1970). The meaning of “increasing the biosynthetic flux” is clear when read in light of the specification, which provides examples of increased tocopherol and a description of increases, decreases, and modulation of ratios of tocopherol compounds.

As such, it is submitted that claim 29 complies with 35 U.S.C. § 112, 2nd paragraph, and withdrawal of this rejection is respectfully requested.

V. Rejection under 35 U.S.C. §102

Claims 1-4, 13-15 and 19-20³ stand rejected under 35 U.S.C. §102 as allegedly being anticipated by Kuntz *et al.*, *The Plant Journal* 2:25-34 (1992). This rejection is respectfully traversed.

As amended, claims 1, 13, 19, and 20 are not anticipated by Kuntz *et al.* Whatever else Kuntz *et al.* may disclose, Kuntz *et al.* fail to disclose an isolated nucleic acid molecule encoding a prenyltransferase having a nucleic acid sequence comprising SEQ ID NO:1. Nor does Kuntz *et al.* disclose a method for producing a tocopherol compound in a host cell, a method for alteration of a tocopherol content in a host cell or a method for increasing the biosynthetic flux in a cell by transforming a host cell with a DNA encoding a prenyltransferase.

As such, it is submitted that the claims are patentable over Kuntz *et al.*, and withdrawal of this rejection is respectfully requested.

Claims 1-4, 13-16, 19-20 and 34⁴ also stand rejected under 35 U.S.C. §102 as allegedly being anticipated by Zhu *et al.*, *Plant Molecular Biology* 35:331-341 (1997). The Examiner contends that this reference anticipates claims 1-4 and 13-16, 19-20 and 34. This rejection is respectfully traversed.

³ Applicants have cancelled claims 2-4, and 14-15 without prejudice to facilitate prosecution. Claims 1, 13, 19, and 20 therefore stand rejected under 35 U.S.C. §102.

⁴ Applicants have cancelled claims 2-4, 14-16, and 34 without prejudice to facilitate prosecution. Claims 1, 13, 19, and 20 therefore stand rejected under 35 U.S.C. §102.

The Examiner states that Zhu *et al.* teach isolated nucleic acid constructs encoding a prenyltransferase from *Arabidopsis*. Whatever else Zhu *et al.* may disclose, Zhu *et al.* fail to disclose an isolated nucleic acid molecule encoding a prenyltransferase having a nucleic acid sequence comprising SEQ ID NO: 1. Nor does Zhu *et al.* disclose a method for producing a tocopherol compound in a host cell, a method for alteration of a tocopherol content in a host cell or a method for increasing the biosynthetic flux in a cell by transforming a host cell with a DNA encoding a prenyltransferase.

As such, it is submitted that the claims are patentable over Zhu *et al.*, and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the above, each of the presently pending claims is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections and to pass the application to issue. The Examiner is invited to contact the undersigned at (202) 942-5000 with respect to any unresolved issues remaining in this application.

Applicants do not believe that any fees are due at this time other than those provided for in the accompanying papers; however, should any fees be required for any reason relating to this document, the Commissioner is authorized to deduct the fees from Arnold & Porter Deposit Account No. 50-1824, referencing attorney docket number 16516.105.

Respectfully submitted,



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Marked Up Specification

Page 5, lines 6-9:

Figure 25 provides a bar graph of HPLC analysis of seed extracts from *Arabidopsis* plants transformed with pCGN10803 (35S-ATPT2, in the antisense orientation), pCGN10802 (line 1625, napin ATPT2 in the sense orientation), pCGN10809 (line 1627, 35S-ATPT3 in the sense orientation), a nontransformed (wt) [constrol] control, and an empty vector transformed control.

Page 42, lines 10-11:

Results of the HPLC analysis of seed extracts of transgenic *Arabidopsis* lines containing pMON10822 for the expression of [ATAT2] ATPT2 from the napin promoter are provided in Figure 24.

Page 42, lines 12-15:

HPLC analysis results of *Arabidopsis* seed tissue expressing the [ATAT2] ATPT2 sequence from the napin promoter (pMON10822) demonstrates an increased level of tocopherols in the seed. Total tocopherol levels are increased as much as 50 to 60% over the total tocopherol levels of non-transformed (wild-type) *Arabidopsis* plants (Figure 24).

Page 42, lines 16-23:

Furthermore, increases of particular tocopherols are also increased in transgenic *Arabidopsis* plants expressing the [ATAT2] ATPT2 nucleic acid sequence from the napin promoter. Levels of delta tocopherol in these lines are increased greater than 3 fold over the delta tocopherol levels obtained from the seeds of wild type *Arabidopsis* lines. Levels of gamma tocopherol in transgenic *Arabidopsis* lines expressing the [ATAT2] ATPT2 nucleic acid sequence are increased as much as about 60% over the levels obtained in the seeds of non-

transgenic control lines. Furthermore, levels of alpha tocopherol are increased as much a 3 fold over those obtained from non-transgenic control lines.

Page 42, lines 24-26:

Results of the HPLC analysis of seed extracts of transgenic *Arabidopsis* lines containing pMON10803 for the expression of [ATAT2] ATPT2 from the enhanced 35S promoter are provided in Figure 25.

Marked Up Claims

1. (Amended) An isolated nucleic acid sequence encoding a prenyltransferase wherein said nucleic acid sequence comprises SEQ ID NO: 1.

13. (Amended) A nucleic acid construct comprising as operably linked components, a transcriptional initiation region functional in a host cell, a nucleic acid sequence encoding a prenyltransferase, wherein said nucleic acid sequence comprises SEQ ID NO: 1, and a transcriptional termination region.

18. (Amended) A plant cell comprising [the construct of Claim 13] a nucleic acid construct that comprises as operably linked components, a transcriptional initiation region functional in a host cell, a nucleic acid sequence encoding a prenyltransferase, wherein said nucleic acid sequence comprises SEQ ID NO: 1, and a transcriptional termination region.

24. (Amended) A method for producing a tocopherol compound [of interest] in a host cell, said method comprising obtaining a transformed host cell, said host cell having and expressing in its genome:

a construct having a DNA sequence encoding a prenyltransferase operably linked to a transcriptional initiation region functional in a host cell,
wherein said prenyltransferase is involved in the synthesis of tocopherols.

36. (Amended) [The DNA sequence of Claim 4] An isolated nucleic acid molecule encoding a prenyltransferase wherein said prenyltransferase is from corn.

39. (Amended) [The DNA sequence of Claim 4] An isolated nucleic acid molecule encoding a prenyltransferase wherein said prenyltransferase is from soybean.